REMARKS

Claims 53, 55-58 and 60-63 are pending in this application. Claims 53 and 58 have been amended. No new matter has been added.

35 U.S.C. § 103 rejection

Claims 53, 55-58 and 60-63 stand rejected under 35 U.S.C. § 103(a) as being obvious over U.S Patent No. 5,648,059 ('059); U.S Patent No. 5,843,894 ('894); and Hammond et al. The Examiner asserts that '059 teaches L-lysine, arginine and ornithine as useful to inhibit the retention and reabsorption of therapeutic immunoconjugates, such as antibodies and monoclonal antibodies, and also teaches decreased protein uptake by the kidney when 10 mg of lysine is administered. The Examiner also asserts that '894 teaches D-lysine as useful for reducing the uptake of antibody fragments and that the effective dosage of a lysine and polylysine solution in reducing uptake of antibody fragments is 2-35 g/L and 10-25 g/L, respectively. The Examiner further asserts that Hammond et al. teach 4.93 g/L of lysine and 17.6 g/L of arginine as useful in blocking renal tubular uptake of somatostatin. The Examiner acknowledges, however, that the above references do not expressly teach the claimed dosage of lysine and arginine or the use of lysine and arginine together. In addition, the Examiner points out that the method of the claimed invention contains the phrase "comprising," which is an open-ended transitional phrase that permits anything other than lysine and arginine to be employed in the claimed method.

Claims 53 and 58 have been amended to recite the transitional phrase "consisting essentially of" instead of "comprising." Use of the transitional phrase "consisting essentially of" limits the scope of the claims to lysine and arginine or ornithine, and to any other amino acid which does not materially affect the basic and novel characteristics of the claimed invention. *In re Herz,* 537 F.2d 549, 551-52 (CCPA 1976). Applicants point out, for the reasons provided below, that amino acids other than lysine and arginine or ornithine would materially affect the basic and novel characteristics of the claimed invention, and thus the scope of the claims would effectively be limited to lysine and arginine or ornithine.

Specifically, Hammond et al. teach the administration of Synthamin 14 without electrolytes, an amino acid preparation which happens to contain lysine and arginine along with thirteen other amino acids. Thus, Hammond et al. do not teach nor suggest the co-administration of lysine and arginine. Furthermore, as stated in the present application, these amino acid cocktails usually comprise a total amount of about 100 grams or more of various amino acids which can cause severe hyperkalemia and which can lead to acute and life-threatening cardiotoxicity, an adverse effect that the novel co-administration of lysine and arginine or ornithine in low dosages of the claimed invention avoids.

With respect to the '059 patent, it discloses administering an effective amount of a single non-target reduction moiety, in which the preferred non-target reduction moiety is lysine and functional constituents or derivatives thereof. Nowhere does the '059 patent teach or suggest administering lysine in combination with arginine or ornithine. Although the '059 patent teaches that other moieties can include "ornithine, arginine, epsilon amino caproic acid, cyclocaprone and the like" (Column 5, lines 18-19), as stated above, it does not teach or suggest co-administering lysine with any other non-target reduction moiety. Indeed, the '059 patent actually teaches away from co-administering lysine with another amino acid. Specifically, at column 5, lines 20-21, it is stated that "lysine is the preferred non-target reduction moiety for use in the present invention," and thus teaches away from combining lysine with other amino acids generally, or with arginine or ornithine in particular. Furthermore, as discussed in the present application (on page 3, line 13 to page 4, line 3), there are several disadvantages to administering lysine alone. In particular, Applicants have demonstrated that L-lysine administration in humans in an effective total dose of 75 grams may cause severe hyperkalemia which may result in acute and life-threatening cardiotoxicity. Applicants submit that the disclosure of lysine administration alone, along with a list of other agents which may be substituted for lysine, does not teach or suggest the co-administration of lysine and arginine or ornithine in specific low dosage amounts which results in the new and unexpected synergistic effects of the claimed invention.

With respect to the '894 patent, it teaches a method of reducing kidney uptake of antibody fragment conjugates by administration of lysine, either alone or as a mixture of at least

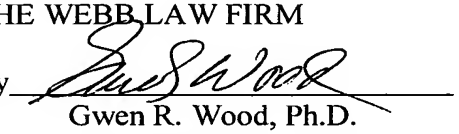
two of D-lysine, poly-D-lysine or poly-L-lysine. Nowhere does the '894 patent teach or suggest the co-administration of specific low dosage amounts of lysine and arginine or ornithine.

In conclusion, Applicants respectfully submit that neither the '059 patent, the '894 patent, nor Hammond et al., either alone or in combination, teaches or suggests the new and unexpected findings of the method and therapeutic composition of the claimed invention, namely, the administration to a patient of a combination of two specific amino acids, e.g., lysine and arginine or ornithine, which co-administration shows a surprising synergistic effect. Thus, lower doses of the two co-administered amino acids are needed, which effectively inhibits renal uptake of proteins and peptides which can damage the kidneys and cause other serious adverse effects.

In view of the foregoing amendments and remarks, it is respectfully submitted that all pending claims 53, 55-58 and 60-63 in the present application are distinguishable from the cited prior art. Accordingly, reconsideration and withdrawal of the rejection and an early Notice of Allowance are respectfully requested.

Respectfully submitted,

THE WEBB LAW FIRM

By 

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